Myocardial Triglyceride in Health and in Metabolic Disease

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Introduction

Obesity and type 2 diabetes are associated with elevated plasma lipids and hypertension and constitute important causes of cardiovascular morbidity and mortality. These traditional cardiac risk factors alone do not fully explain poor cardiovascular outcome in patients with type 2 diabetes. An emerging body of basic research has advanced the novel concept of cardiac lipotoxicity (1, 2, 3). Ectopic deposition of triglyceride droplets in cardiac myocytes is thought to activate adverse signaling pathways that culminate in left ventricular dysfunction. We previously tested and evaluated localized magnetic resonance spectroscopy technique to measure intra-myocardial triglyceride (mTG) in vivo (4, 5). This technological breakthrough allows translating the basic research from genetic rodent models to human obesity and type 2 diabetes. We hypothesized that cardiac lipotoxicity constitutes a major new mechanism in the early pathogenesis of human diabetic heart disease. We tested our hypothesis by evaluating mTG as well as cardiac geometry and function in vivo in people with varying levels of glucose tolerance and insulin sensitivity.

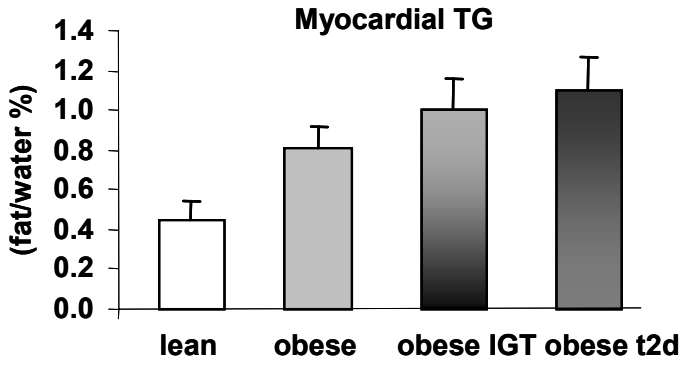
Subjects & Methods

We studied 59 people from three major ethnic groups and both genders (32 women) residing in Dallas County. Study participants characteristics are summarized in Table. Each participant underwent: 1) oral glucose tolerance test in outpatient GCRC unit, 2) cardiac MRI for cardiac mass and function assessment (ejection fraction - EF and peak filling rate PFR), and 3) cardiac ^{1}H-MRS for evaluation of mTG. MTG content was determined in the ventricular septum using cardiac triggering and respiratory gating on 1.5T Philips Clinical Scanner. For data analysis we divided study participants into four groups: 1) lean; 2) obese; 3) obese with Impaired Glucose Tolerance (IGT), 4) obese with type 2 diabetes. All diabetic patients were not aware of their medical condition prior to evaluation.

mean ± std error	lean	obese	obese IGT	obese t2d
N	12	21	17	9
AGE(years)	35±4	38±3	50±2	51±3
BMI (kg/m2)	22±1	31±1	31±1	36±2
fasting Glu (mg/dL)	89±3	90±3	99±3	108±4
2 hours Glu (mg/dL)	92±5	99±5	163±5	226±7
fasting Insulin (u)	3±1	7±2	6±1	22±10
2 hours Insulin (u)	24±8	34±6	95±17	131±25

Results and Discussion

We have observed incremental increase of mTG with elevation of obesity and development of glucose intolerance, and diabetes. Myocardial triglyceride levels were the lowest in lean and the highest in obese diabetic individuals but the largest difference in mTG content was observed between lean and obese individuals (~100%). The figure on left summarizes our findings. Our results reflect the outcomes from animal studies that demonstrate increased mTG in models of obesity and type 2 diabetes. Interestingly, we did not observe mTG was not related with any measures of left ventricular function including as EF and PFR at rest. It is possible that EF and PFR are not sensitive enough to test subtle changes in heart function as it adapts efficiently to new metabolic conditions. In conclusion, it appears as though myocardial triglyceride deposition in humans is positively related to obesity and glucose tolerance. These data are strikingly similar to studies in rodents which have demonstrated that myocardial steatosis is a pathological consequence of obesity and type 2 diabetes providing initial clinical evidence for myocardial steatosis in human obesity and type 2 diabetes.



References:

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